Paclitaxel and Carboplatin in Elderly Patıents with Advanced Non-Small Cell Lung Cancer

Yaşlı İleri Evre Küçük Hücreli Dışı Akciğer Kanserli Hastalarda Paklitaksel ve Karboplatin

Yaşlı Akciğer Kanserli Hastalarda Kemoterapi / Chemotherapy in Elderly Lung Cancer Patients

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Özet

Amaç: Bu çalışmada, ileri evre yaşlı küçük hücreli dışı akciğer kanseri (KHDAK) hastalarında, paklitaksel ve karboplatin (PK) rejiminin etkinliği ve tolerabilitesi araştırıldı. Gereç ve Yöntem: Evre IIIB (n=11) veya IV (n=34) KHDAK nedeniyle PK tedavisi alan yaşlı (yaş ≥ 70) 45 hasta retrospektif olarak değerlendirildi. Bulgular: Hastaların 43'ü erkek, 2'si kadın olup ortanca yaşı 75.5 (70-82) idi. Yanıt oranı %40'dı. Medyan genel sağkalım süresi ve progresyonsuz sağkalım süresi sırasıyla 13 ay ve 8.5 ay, 1-yıllık sağkalım oranı %51'di. Tedavi hastalar tarafından iyi tolere edildi. Grade 3 veya 4 nötropeni (%57.7) en sık görülen yan etkiydi. Tedaviye bağlı ölüm görülmedi. Sonuç: PK rejimi ileri evre yaşlı KHDAK hastalarının tedavisi için iyi bir alternatif olabilir.

Anahtar Kelimeler

Karsinom; Küçük Hücreli Dışı; Akciğer; Yaşlı; Kemoterapi

Abstract

Aim: In this study, the safety and tolerability of paclitaxel and carboplatin (PC) regimen in elderly patients with advanced non-small cell lung cancer (NSCLC) was investigated. Material and Method: Elderly patients (ages ≥70 years) who received PC for stage III (n=11) or IV (n=34) NSCLC were evaluated retrospectively. Results: There were 43 males and 2 females, with a median age of 75.5 (range, 70-82). The response rate was 40%. The median overall survival time and progression-free survival time was 13 months and 8.5 months, respectively. One-year survival rate was 51%. Treatment was well tolerated by the patients. The most frequent side effect observed was grade 3 or 4 neutropenia (57.7%). There was no treatment-related death. Discussion: PC regimen may be a good alternative for the treatment of elderly patients with advanced NSCLC.

Keywords

Carcinoma; Non-Small Cell; Lung; Elderly; Chemotherapy

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Introduction

Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer. At the time of diagnosis, the majority of NSCLC patients already have advanced disease. More than 50% of NSCLC patients are diagnosed over the age of 65 and about 30% over the age of 70 [1]. Systemic chemotherapy plays a critical role in improving survival and remains a therapeutic option in elderly patients with advanced NSCLC. However, age-related decreases in organ function, including reductions in renal, hepatic, and bone marrow function, have the potential to increase toxicity of chemotherapy in the elderly. Therefore, the treatment of elderly patients with advanced NSCLC represents a considerable challenge for the practitioner of oncology. The best chemotherapy regimen for elderly patients with advanced NSCLC is still debated. A recent International expert panel suggested that single-agent chemotherapy with a third-generation drug (e. g, vinorelbine, gemcitabine and taxanes) should be recommended option for unselected elderly NSCLC patients [2].

Platinum-based chemotherapy is currently recommended as the standard therapy for patients with advanced NSCLC and the combination of paclitaxel and carboplatin (PC) is one of the most commonly used chemotherapy regimens for this disease. During the past decade, a number of patients 70 years of age and over with locally advanced and metastatic NSCLC received PC regimen at our hospital. In the present study, we reviewed our experience between 2004 and 2008, with elderly patients treated with PC.

Material and Method

We performed a detailed retrospective review of the medical records of patients aged ≥70 years with stage IIIB or IV NSCLC who received PC regimen between January 2004 and August 2008 at our hospital. The data on demographic information, number of chemotherapy cycles, toxicity, response, and date of disease progression and death were collected. All patients were staged on the basis of physical examination, chest radiography, computed tomography (CT) scan of chest, abdomen, and brain, radionuclide scan of bone, and positron emission tomography. All patients had histologically or cytologically proven NSCLC, and had radiologically measurable disease and adequate hematologic, renal and hepatic function.

Paclitaxel was received intravenously (i.v.) at a dose of 175 mg/m2 over 3 h in 500 ml of normal saline and then carboplatin was received i.v. at an AUC of 6 mg/ml/min over 60 min in 250 ml of normal saline on day 1. Before the administration of paclitaxel, the patients were premedicated with dexamethasone (20 mg i.v.), ranitidine (50 mg i.v.) and feniramin (45.5 mg i.v.). A 5-HT3 receptor antagonist was also i.v. administered immediately before paclitaxel infusion. Chemotherapy courses were repeated every three or four weeks. Patients were treated for a maximum of six cycles or until intolerable toxicity, disease progression, or death. Prophylactic hematologic growth factors were not administered routinely.

Chest radiography was obtained before each cycle, and CT scans were performed every two or three cycles to evaluate the response to chemotherapy. Tumor response was assessed according to World Health Organization (WHO) criteria. Toxicity was assessed using WHO criteria and the worst toxicity grade for each patient in all cycles of chemotherapy was recorded. Overall survival was calculated from the date of the first cycle of chemotherapy to the date of death from any cause or last follow-up visit. Progression-free survival was calculated from the date of the first cycle of chemotherapy to the first evidence of progression. Survival times were estimated using Kaplan-Meier method.

Results

Of 52 patients received PC regimen, 45 were assessable. Seven patients were excluded from the study because of insufficient clinical data. There were 43 men and 2 women. The median age was 75.5 years (range, 70-82). Patient characteristics are summarized in Table 1. Eastern Cooperative Oncology Group performance scores were 1 in 24 (53.3%) patients, 0 in 14 (31%), and 2 in 7 (15.5%) patients. Comorbidity consisted of hypertension (33%), chronic obstructive pulmonary disease (17%), and diabetes (13%). Twenty-three patients had squamous cell carcinoma, 11 had adenocarcinoma, and 1 had large cell carcinoma. The histologic subtype of NSCLC was not defined in 10 patients. Thirty four patients had stage IV (75.5%) and 11 (24.5%) had stage IIIB disease (with pleural effusion or N3 nodal disease) at the time of diagnosis. More than half the patients with stage IV disease had two or more disease sites.

Response and survival

The median number of chemotherapy cycles received was four (range, 1-6). The response could not be evaluated in 3 patients because of early death. The overall response rate was 40%. One patient (2%) had a complete response, and 16 (38%) had a partial response.

The median follow up time from diagnosis was 11.8 months. The median overall survival (OS) time was 13 months (95% CI, 9.9-16), and 1-year survival rate was 51%. The median progression-free survival (PFS) time was 8.5 months (95% CI, 6.7-10.4) and, the 1-year progression- free survival rate was 15.5%.

Toxicity

The most relevant side effects are summarized in Table 2. The incidence of grade 3/4 neutropenia was 57.7%. Six patients

Table 1. Characteristics of the patients

Characteristics	No. of patients (%)
Age (median, 75.5 yrs; range, 70-82)	
70-74 years	25 (55)
75-82 years	20 (45)
Gender	
Male	43 (95.5)
Female	2 (4.5)
ECOG performance status	
0	14 (31)
1	24 (53.3)
2	7 (15.5)
Histology	
Squamous cell carcinoma	23 (51.1)
Adenocarcinoma	11 (24.5)
Large cell carcinoma	1 (2.2)
Unclassified	10 (22.2)
Stage	
IIIB	11 (24.5)
IV	34 (75.5)

Table 2. Chemotherapy toxicity

Toxicity	Grade 1-2	Grade 3-4
	n (%)	n (%)
Neutropenia	16 (35.5)	26 (57.7)
Anemia	28 (62)	8 (17.7)
Thrombocytopenia	27 (60)	8 (17.7)
Nausea/vomiting	30 (66.6)	0 (0)
Neuropathy	21 (47)	0 (0)
Myalgia/arthralgia	15 (33)	2 (4.4)
Diarrhea	3 (6.6)	0 (0)

were hospitalized for febrile neutropenia. Granulocyte-colony stimulating factor was used in nearly 60% of the patients. The incidences of grade 3/4 anemia and thrombocytopenia were relatively low. Twenty-one patients (46.7%) had grade 1/2 neuropathy. No treatment-related death was observed.

Discussion

In this retrospective study, we evaluated the efficacy and toxicity of PC regimen in elderly patients with advanced NSCLC. The rate of response to PC was 40%. The median PFS and OS times were 8.5 months and 13 months, respectively. These results are comparable with those of other studies investigating activity of PC in non-elderly patients [3, 4]. PC was well tolerated in our patients. Side effects were generally manageable and did not have a significant impact on the quality of life in patients. As expected, hematological toxicity was frequent. Nearly 60% of our patients experienced grade 3 or 4 neutropenia. However, the hematological toxicity was readily managed and of short duration and did not result in any treatment-related deaths.

In a phase II study, Okamoto et al. [5] investigated the efficacy and safety of PC in 25 patients aged ≥70 years with chemotherapy-naive advanced NSCLC. The paclitaxel dose 180 mg/m2) and carboplatin doses (AUC=5) they used were slightly different from that used in our study. On the other hand, they excluded patients if they had an ECOG performance score greater than 1. The results of this study were similar to those in our study. The median survival time was 12.3 months, and the 1-year survival rate was 52%. In a phase II study conducted by Inoue et al. [6], 40 elderly NSCLC patients received paclitaxel at a dose of 70 mg/m2 on days 1, 8, 15, and carboplatin at the target dose of AUC of six on day 1 every 28 days. The overall response rate was 45%. The median survival time was 14 months and the 1-year survival rate was 62%. The relatively high rate of hematological toxicity was observed in this study. Grade 3 or 4 neutropenia was experienced in 70% of the patients. Subsequently, the same authors designated a randomized trial comparing the efficacy and safety of these two schedules of PC regimen in elderly patients (≥70 years) with advanced NSCLC [7]. Patients were randomly assigned to either the weekly arm (70 mg/m2 paclitaxel on days 1, 8, 15, and carboplatin AUC=6 on day 1) or the standard arm (200 mg/m2 paclitaxel and carboplatin AUC=6 on day 1). The overall response rate and median PFS were 55% and 6 months for the weekly arm and 53% and 5.6 months for the standard arm. Regarding the safety, the weekly regimen was less toxic than the standard regimen. Grade 3-4 neutropenia and peripheral neuropathy were observed in 41% and 0% of the patients in the weekly arm and 88% and 25% in the standard arm, respectively. These results are supported by Ramalingam et al [8]. They reported similar survival and response rates between the weekly regimen and standard regimen of PC for elderly patients with advanced NSCLC.

Several clinical trials using other chemotherapy drugs have been reported recently for elderly patients with advanced NSCLC [9-13]. The response rates for non-platinum-based single or double-agent chemotherapeutics regimens in these studies ranged from 16 to 23%, with 1-year survival rates of 27-45%. The response rate of 40% and 1-year survival rate of 51% detected in our study thus higher than values obtained in these studies.

We concluded that PC regimen can be used safely and effectively in the treatment of elderly patients with advanced NSCLC. The weekly regimen could be considered a good alternative to standard 3-weekly regimen in these patients.

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